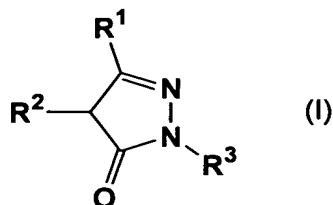


CLAIMS

1. A blood-brain barrier disruption inhibitor which comprises as an active ingredient a pyrazolone derivative represented by the following formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:



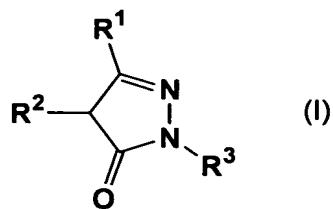
wherein R¹ represents a hydrogen atom, an aryl group, a C₁₋₅ alkyl group, or a C₃₋₆ (total carbon number) alkoxy carbonylalkyl group; R² represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C₁₋₅ alkyl group or a C₁₋₃ hydroxyalkyl group; or R¹ and R² are combined with each other to represent C₃₋₅ alkylene group; and R³ represents a hydrogen atom, a C₁₋₅ alkyl group, a C₅₋₇ cycloalkyl group, a C₁₋₃ hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C₁₋₅ alkyl group, a C₁₋₅ alkoxy group, a C₁₋₃ hydroxyalkyl group, a C₂₋₅ (total carbon number) alkoxy carbonyl group, a C₁₋₃ alkylmercapto group, a C₁₋₄ alkylamino group, a C₂₋₈ (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

2. The blood-brain barrier disruption inhibitor according to claim 1 which has an action of inhibiting increases in permeability of the blood-brain barrier.

3. The blood-brain barrier disruption inhibitor according to claim 1 or 2 which has an action of inhibiting increases in the amount of inflammatory cytokines in spinal fluid.

4. The blood-brain barrier disruption inhibitor according to any of claims 1 to 3 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

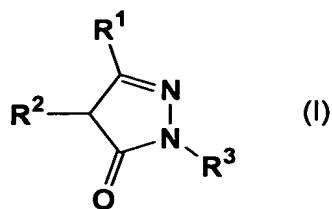
5. A medicament for prevention and/or treatment of multiple sclerosis, meningitis, cerebritis or brain abscess, which comprises as an active ingredient a pyrazolone derivative represented by the above-described formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:



wherein R¹ represents a hydrogen atom, an aryl group, a C₁₋₅ alkyl group, or a C₃₋₆ (total carbon number) alkoxy carbonyl alkyl group; R² represents a hydrogen atom, an aryloxy group, an aryl mercapto group, a C₁₋₅ alkyl group or a C₁₋₃ hydroxy alkyl group; or R¹ and R² are combined with each other to represent C₃₋₅ alkylene group; and R³ represents a hydrogen atom, a C₁₋₅ alkyl group, a C₅₋₇ cycloalkyl group, a C₁₋₃ hydroxy alkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C₁₋₅ alkyl group, a C₁₋₅ alkoxy group, a C₁₋₃ hydroxy alkyl group, a C₂₋₅ (total carbon number) alkoxy carbonyl group, a C₁₋₃ alkyl mercapto group, a C₁₋₄ alkyl amino group, a C₂₋₈ (total carbon number) dialkyl amino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

6. The medicament according to claim 5 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

7. A method for inhibiting a blood-brain barrier disruption which comprises a step of administering to mammals such as a human, an effective amount of a pyrazolone derivative represented by the formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:



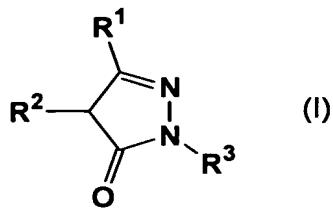
wherein R¹ represents a hydrogen atom, an aryl group, a C₁₋₅ alkyl group, or a C₃₋₆ (total carbon number) alkoxy carbonyl alkyl group; R² represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C₁₋₅ alkyl group or a C₁₋₃ hydroxy alkyl group; or R¹ and R² are combined with each other to represent C₃₋₅ alkylene group; and R³ represents a hydrogen atom, a C₁₋₅ alkyl group, a C₅₋₇ cycloalkyl group, a C₁₋₃ hydroxy alkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C₁₋₅ alkyl group, a C₁₋₅ alkoxy group, a C₁₋₃ hydroxy alkyl group, a C₂₋₅ (total carbon number) alkoxy carbonyl group, a C₁₋₃ alkylmercapto group, a C₁₋₄ alkylamino group, a C₂₋₈ (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

8. The method according to claim 7 wherein the blood-brain barrier disruption is inhibited by inhibiting increases in permeability of the blood-brain barrier.

9. The method according to claim 7 or 8 wherein the blood-brain barrier disruption is inhibited by inhibiting increases in the amount of inflammatory cytokines in spinal fluid.

10. The method according to any of claims 7 to 9 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

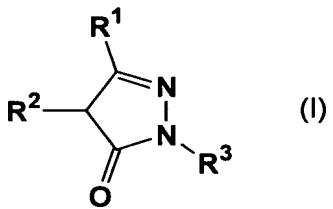
11. A method for preventing and/or treating multiple sclerosis, meningitis, cerebritis or brain abscess which comprises a step of administering to mammals such as a human, an effective amount of a pyrazolone derivative represented by the formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof:



wherein R¹ represents a hydrogen atom, an aryl group, a C₁₋₅ alkyl group, or a C₃₋₆ (total carbon number) alkoxycarbonylalkyl group; R² represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C₁₋₅ alkyl group or a C₁₋₃ hydroxyalkyl group; or R¹ and R² are combined with each other to represent C₃₋₅ alkylene group; and R³ represents a hydrogen atom, a C₁₋₅ alkyl group, a C₅₋₇ cycloalkyl group, a C₁₋₃ hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C₁₋₅ alkyl group, a C₁₋₅ alkoxy group, a C₁₋₃ hydroxyalkyl group, a C₂₋₅ (total carbon number) alkoxycarbonyl group, a C₁₋₃ alkylmercapto group, a C₁₋₄ alkylamino group, a C₂₋₈ (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

12. The method according to claim 11 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

13. Use of a pyrazolone derivative represented by formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof, for the production of a blood-brain barrier disruption inhibitor;



wherein R¹ represents a hydrogen atom, an aryl group, a C₁₋₅ alkyl group, or a C₃₋₆ (total carbon number) alkoxycarbonylalkyl group; R² represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C₁₋₅ alkyl group or a C₁₋₃ hydroxyalkyl group; or R¹

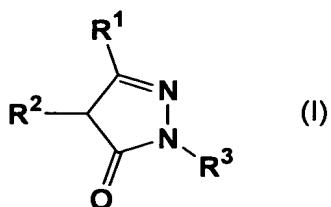
and R² are combined with each other to represent C₃₋₅ alkylene group; and R³ represents a hydrogen atom, a C₁₋₅ alkyl group, a C₅₋₇ cycloalkyl group, a C₁₋₃ hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C₁₋₅ alkyl group, a C₁₋₅ alkoxy group, a C₁₋₃ hydroxyalkyl group, a C₂₋₅ (total carbon number) alkoxy carbonyl group, a C₁₋₃ alkylmercapto group, a C₁₋₄ alkylamino group, a C₂₋₈ (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

14. The use according to claim 13 wherein the blood-brain barrier disruption inhibitor has an action of inhibiting increases in permeability of the blood-brain barrier.

15. The use according to claim 13 or 14 wherein the blood-brain barrier disruption inhibitor has an action of inhibiting increases in the amount of inflammatory cytokines in spinal fluid.

16. The use according to any of claims 13 to 15 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.

17. Use of a pyrazolone derivative represented by formula (I) or a physiologically acceptable salt thereof, or a hydrate thereof or a solvate thereof, for the production of a medicament for prevention and/or treatment of multiple sclerosis, meningitis, cerebritis or brain abscess:



wherein R¹ represents a hydrogen atom, an aryl group, a C₁₋₅ alkyl group, or a C₃₋₆ (total carbon number) alkoxy carbonylalkyl group; R² represents a hydrogen atom, an aryloxy group, an arylmercapto group, a C₁₋₅ alkyl group or a C₁₋₃ hydroxyalkyl group; or R¹ and R² are combined with each other to represent C₃₋₅ alkylene group; and R³ represents

a hydrogen atom, a C₁₋₅ alkyl group, a C₅₋₇ cycloalkyl group, a C₁₋₃ hydroxyalkyl group, a benzyl group, a naphthyl group, a phenyl group, or a phenyl group substituted with the same or different 1 to 3 substituents selected from the group consisting of a C₁₋₅ alkyl group, a C₁₋₅ alkoxy group, a C₁₋₃ hydroxyalkyl group, a C₂₋₅ (total carbon number) alkoxy carbonyl group, a C₁₋₃ alkyl mercapto group, a C₁₋₄ alkylamino group, a C₂₋₈ (total carbon number) dialkylamino group, a halogen atom, a trifluoromethyl group, a carboxyl group, a cyano group, a hydroxyl group, a nitro group, an amino group and an acetamide group.

18. The use according to claim 17 wherein the pyrazolone derivative represented by the formula (I) is 3-methyl-1-phenyl-2-pyrazolin-5-one.